REMARKS

A. Claim objections

Claims 206-207, 270-271, 274-277, and 280-283 are objected to under 37 C.F.R. 1.75 as being a substantial duplicate of claims 190-191. Applicant has canceled claims 190-191, 206-207, 270-271, 274-277, and 280-283, rendering this objection moot.

Claims 248-249 and 272-273 are objected to under 37 C.F.R. 1.75 as being a substantial duplicate of claims 234-235. The Office Action states that these claims are all drawn to a method comprising human IMPDH type II protein and mammalian cells. However, Applicant contends that this characterization is incorrect. Claims 234-235 are drawn to a method comprising eukaryotic cells, but contain no reference to mammalian cells. Claims 248-249 and 272-273, on the other hand, are drawn to mammalian cells. Thus, Applicant has canceled claims 272-273 while leaving claims 234-235 and 248-249 intact.

Claims 260-261, 278-279, and 284-285 are objected to under 37 C.F.R. 1.75 as being a substantial duplicate of claims 219-220. Applicant has canceled claims 260-261, 278-279, and 284-285, leaving only claims 219-220 from this group of claims.

B. Rejection under 35 U.S.C. 103

Claims 73-74, 142-143, 190-191, 206-207, 219-220, 234-235, 248-249, 260-261, and 270-285 are rejected under 35 U.S.C. 103 as obvious over Farazi et al. in view of Lightfoot et al. and Roelant et al. Applicant has canceled claims 190-191, 206-207,

260-261, 270-279, and 282-285, rendering the rejection moot with regards to these claims.

According to the Office Action, Farazi teaches mutants of human IMPDH type II that are resistant to inhibitors of wildtype IMPDH, and further teaches that IMPDH inhibitors have antiproliferative activity. The Office Action goes on to state that "Farazi et al. teach that mutant IMPDH which are resistant to MPA can be very useful in anti-infective chemotherapy" (Office Action, page 4).

Applicant asserts that this is a mischaracterization of the cited statement in Farazi. The statement actually reads "differences in the properties of microbial and mammalian IMPDHs suggest that species-selective IMPDH inhibitors can be designed, which will be useful for anti-infective chemotherapy." Thus, Farazi is suggesting the use of species-specific IMPDH *inhibitors* in anti-infective chemotherapy, not the use of IMPDH mutants. MPA is an inhibitor of mammalian IMPDH but not microbial IMPDH (Farazi, abstract). The Farazi IMPDH mutants were used to identify regions of IMPDH that cause this species specificity. The purpose of this work was to eventually design species-specific IMPDH inhibitors.

According to the Office Action, "the only difference between the mutant of the instant invention and wild type IMPDH II is at residues 333 and 351" (Office Action, page 4). Applicant asserts that this statement applies only to the IMPDH mutant having the amino acid sequence set forth in SEQ ID NO. 4. The other claimed IMPDH mutant of the present invention comprises "the amino acid sequence set forth in SEQ ID NO. 4 containing an alanine at amino acid position 190 and a glycine at amino acid position

191. Thus, this IMPDH mutant differs from wild type IMPDH at resides 190, 191, 333, and 351.

The Office Action goes on to state that "it would have been obvious...to make two mutations with human IMPDH type II and screen whether the mutants have resistance against inhibitors of IMPDH by performing cell proliferation assays" (Office Action, page 5). According to the Office Action, the motivation for applying the teachings of Lightfoot to human IMPDH is for "potential use of the mutant enzyme in human, such as for anti-infective chemotherapy," or for the development of species-specific IMPDH inhibitors.

Applicant respectfully asserts that neither of the motivations posited by the Office Action existed at the time of the invention. As stated above, Farazi does not teach the use of mutant IMPDH in anti-infective chemotherapy. Rather, Farazi teaches the use of species-specific IMPDH *inhibitors* in anti-infective chemotherapy. As for developing those species-specific inhibitors, Farazi merely provides an *E. coli*-based screening method for identifying IMPDH mutants that are resistant to IMPDH inhibitors. Farazi introduced random mutations into IMPDH in *E. coli* and identified mutants that conferred inhibitor resistance. Once identified, the only use contemplated for these mutants is to "explore the structural basis of the species selectivity of MPA" (Farazi, page 962). By identifying structural determinants of inhibitor sensitivity, Farazi suggests that species-specific inhibitors can be developed that preferentially target either microbial or mammalian IMPDH. Inhibitors developed for this purpose would be tested and used on microbial or mammalian cells containing wild-type IMPDH, to determine whether they can selectively inhibit IMPDH from a particular species. Farazi teaches no

use for their IMPDH mutants beyond the development of inhibitors, and certainly does not teach or suggest the introduction of previously identified IMPDH mutants into a cell to selectively proliferate that cell.

In addition to a lack of motivation to combine the Farazi and Lightfoot references, Applicant asserts that there is no teaching or suggestion in either reference to do so. Further, a person of skill in the art would have no reasonable expectation of success for introducing the mutant IMPDHs of the present invention into a eukaryotic cell to selectively proliferate that cell. Farazi contains a reference to the IMPDH mutant of Lightfoot, but states that "experiments suggest that resistance results from the alteration of Thr^{333}...This residue is strictly conserved in all IMPDHs sequenced to date, and therefore cannot be a determinant of species selectivity" (Farazi, pages 961-962). This statement would actually discourage a person skilled in the art from combining the Lightfoot mutant with the method taught in Farazi. The method of Farazi is taught as a means for identifying structural determinants of species selectivity. Since Farazi states that a substitution at residue 333 "cannot be a determinant of species selectivity," there would be no reason to apply the method of Farazi to the Lightfoot mutant. Even if the references were combined, a person skilled in the art would have no reasonable expectation of success for introducing IMPDH mutants into a eukaryotic cell to selectively proliferate that cell.

In light of the foregoing, Applicant respectfully requests that the obviousness rejection be reconsidered and withdrawn.

C. Other amendments

Applicant has amended claims 73-74 by changing the phrase "mammalian enzyme" to "human IMPDH."

CONCLUSION

In view of the foregoing, it is submitted that the present claims are in condition for allowance. Accordingly, Applicant respectfully requests that a Notice of Allowance be issued.

Respectfully submitted,
Perkins Coie LLP

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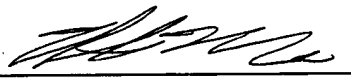

Patrick D. Morris, Ph.D.
Registration No. 53,351

Correspondence Address:
Customer No. 34055
Perkins Coie LLP
P.O.Box 1208
Seattle, WA 98111-1208
Telephone: (310) 788-9900
Facsimile: (310) 788-3399